

AMENDMENTS TO THE CLAIMS:

This listing of claims will replace all prior versions, and listings of claims in the application:

LISTING OF CLAIMS:

1-54 (cancelled)

55. (new): A genetically modified rodent all of whose cells comprise a Serca ATPase gene modified by inserted recombination sites, the modification being homozygous.

56. (new): The rodent of claim 55 comprising several copies of the modified Serca ATPase gene.

57. (new): The rodent of claim 55, wherein the Serca ATPase gene is a Serca2 ATPase gene.

58. (new): The rodent of claim 55, wherein the recombination sites are of heterogenous origin.

59. (new): The rodent of claim 58, wherein the heterogenous recombination sites are of non-mammalian origin.

60. (new): The rodent of claim 59, wherein the recombination sites comprise loxP recombination sites.

61. (new): The rodent of claim 55 all of whose cells further comprise a gene encoding a heterogenous recombinase.

62. (new): The rodent of claim 61, wherein the heterogenous recombinase is of non-mammalian origin.

63. (new): The rodent of claim 62, wherein the recombinase is a Cre recombinase.

64. (new): The rodent of claim 61, wherein expression of the recombinase encoding gene is controlled by a regulatory nucleic acid sequence.

65. (new): The rodent of claim 64, wherein the regulatory nucleic acid sequence is inducible.

66. (new): The rodent of claim 65, wherein said regulatory nucleic acid sequence is inducible by tamoxifen.

67. (new): The rodent of claim 61, wherein expression of the recombinase gene is tissue-specific.

68. (new): The rodent of claim 67, wherein expression of the recombinase gene occurs in heart tissue.

69. (new): The rodent of claim 55, wherein the rodent is a mouse.

70. (new): A eukaryotic cell comprising a Serca ATPase gene modified by inserted recombination sites, the modification being homozygous.

71. (new): The cell of claim 70 comprising several copies of the modified Serca ATPase gene.

72. (new): The cell of claim 70, wherein the Serca ATPase gene is a Serca2 ATPase gene.

73. (new): The cell of claim 70, wherein the recombination sites are of heterogenous origin.

74. (new): The cell of claim 70, wherein the heterogenous recombination sites are of non-mammalian origin.

75. (new): The cell of claim 740, wherein the recombination sites comprise loxP recombination sites.

76. (new): The cell of claim 70 further comprising a gene encoding a heterogenous recombinase.

77. (new): The cell of claim 76, wherein the heterogenous recombinase is of non-mammalian origin.

78. (new): The cell of claim 77, wherein the recombinase is a Cre recombinase.

79. (new): The cell of claim 76, wherein expression of the recombinase encoding gene is controlled by a regulatory nucleic acid sequence.

80. (new): The cell of claim 79, wherein the regulatory nucleic acid sequence is inducible.

81. (new): The cell of claim 70, wherein the cell is of mammalian origin.

82. (new): The cell of claim 81, wherein the cell is of non-human mammalian origin.

83. (new): The cell of claim 82, wherein the cell is of rodent origin.

84. (new): The cell of claim 83, wherein the cell is of mouse origin.

85. (new): The cell of claim 70, wherein said cell is an embryonic cell.

86. (new): The cell of claim 70, wherein said cell is a cardiomyocyte.

87. (new): A gene encoding a Serca ATPase modified by inserted recombination sites.

88. (new): The gene of claim 87, wherein the Serca ATPase is a Serca2 ATPase

89. (new): The gene of claim 87, wherein the recombination sites are of heterogenous origin.

90. (new): The gene of claim 89, wherein the heterogenous recombination sites are of non-mammalian origin.

91. (new): The gene of claim 90, wherein the recombination sites comprise loxP recombination sites.

92. (new): The gene of claim 88, wherein said gene is substantially modified as set forth in SEQ ID 1.

93. (new): A vector comprising the gene of claim 33.

94. (new): The vector of claim 93, wherein the vector is based on pBluescript II KS.

95. (new): A method for inducing defective Ca^{2+} handling in a non-human vertebrate, comprising the steps of inducing recombination and inactivation of a Serca ATPase gene.

96. (new): The method of claim 95, wherein the Serca ATPase gene is a Serca2 ATPase gene.

97. (new): The method of claim 95, wherein the Serca gene is inactivated in heart tissue.

98. (new): The method of claim 61, wherein said non-human vertebrate is a genetically modified rodent, all of whose cells comprise a Serca ATPase gene modified by inserted recombination sites, the modification being homozygous, all of

whose cells further comprise a gene encoding a heterogenous recombinase.

99. (new): A method for inducing heart failure in non-human vertebrate, comprising the steps of inducing recombination and inactivation of a Serca ATPase gene in heart tissue.

100. (new): The method of claim 89, wherein the Serca ATPase gene is a Serca2 ATPase gene.

101. (new): The method of claim 89, wherein said vertebrate is the rodent.

102. (new): A method for screening a compound or a mixture of compounds for activity against defective Ca^{2+} handling, comprising the steps of inducing recombination and inactivation of a Serca ATPase gene in a non-human vertebrate; administering the compound or mixture to said mammal before and/or after the induced inactivation of the Serca ATPase gene.

103. (new): The method of claim 102 wherein the Serca ATPase gene is a Serca2 ATPase gene.

104. (new): The method of claim 102, wherein the Serca gene is inactivated in heart tissue.

105. (new): The method of claim 61, wherein said vertebrate is a genetically modified rodent, all of whose cells comprise a Serca ATPase gene modified by inserted recombination sites, the modification being homozygous, all of whose cells further comprise a gene encoding a heterogenous recombinase.

106. (new): A method for screening a compound or a mixture of compounds for activity against heart failure, comprising the steps of inducing recombination and inactivation of a Serca ATPase gene in heart tissue of a non-human vertebrate; administering the compound or mixture to

said mammal before and/or after the induced inactivation of the Serca ATPase gene.

107. (new): The method of claim 106, wherein the Serca ATPase gene is a Serca2 ATPase gene.

108. (new): The method of claim 106, wherein said vertebrate is a genetically modified rodent all of whose cells comprise a Serca ATPase gene modified by inserted recombination sites, the modification being homozygous, all of whose cells further comprise a gene encoding a heterogenous recombinase;
wherein expression of the recombinase gene is tissue-specific;
and
wherein expression of the recombinase gene occurs in heart tissue.